In the Specification:

Paragraph beginning on Page 1, Line 36:

The use of minimally invasive surgical techniques has dramatically affected the methods and outcomes of surgical procedures. Physically cutting through tissue and organs to visually expose surgical sites in conventional "open surgical" procedures causes tremendous blunt trauma and blood loss. Exposure of internal tissues and organs in this manner also dramatically increases the risk of infection. Trauma, blood loss, and infection all combine to extend recovery times, increase the ~~rate~~ extent of complications, and require a more intensive care and monitoring ~~regiment~~ regimen. The result of such open surgical procedures is more pain and suffering, higher procedural costs, and greater risk of adverse outcomes.

Paragraph beginning on Page 2, Line 4:

In sharp contrast, minimally invasive surgical procedures cause little blunt trauma or blood loss and minimize the risk of infection by maintaining the body's natural barriers to infection substantially intact. Minimally invasive surgical procedures result in faster recovery and cause fewer complications than conventional, open, surgical procedures. Minimally invasive surgical procedures, such as laparoscopic, endoscopic, or cystoscopic surgeries, have replaced more invasive surgical procedures in all areas of surgical medicine. Due to technological advancements in areas such as fiber optics, micro-tool fabrication, imaging and material science, the physician performing the operation has easier-to-operate and more ~~cost~~ cost-effective tools for use in minimally invasive procedures. However, there still exist a host of technical hurdles that limit the efficacy and increase the difficulty of minimally invasive procedures, some of which were overcome by the development of sophisticated imaging techniques. As is further detailed below, the present invention offers ~~a yet~~ further ~~advantage~~ advantages in this respect.

Paragraph beginning on Page 3, Line 19:

The first gamma camera capable of recording all points of the image at one time was described by Hal Anger in 1953. Anger used a detector ~~comprised of~~

comprising a NaI(Tl) screen and a sheet of X-ray film. In the late 1950's, Anger replaced the film screen with a photomultiplier tube assembly. The Anger camera is described in Hal O. Anger, "Radioisotope camera in Hine GJ", Instrumentation in Nuclear Medicine, New York, Academic Press 1967, chapter 19. U.S. Patent No. 2,776,377 to Anger, issued in 1957, also describes such a radiation detector assembly.

Paragraph beginning on Page 5, Line 27:

U.S. Patent No. 5,857,463 to Thurston et al. describes further apparatus for tracking a radiopharmaceutical present within the lymph duct and for locating the sentinel node within which the radiopharmaceutical has concentrated. A smaller, straight, hand-held probe is employed carrying two hand actuable switches. For tracking procedures, the probe is moved in an undulatory manner, wherein the location of the radiopharmaceutical-containing duct is determined by observing a ~~graphics~~ graphic readout. When the region of the sentinel node is approached, a switch on the probe device is actuated by the surgeon to carry out a sequence of squelching operations until a small node locating region is defined.

Paragraph beginning on Page 6, Line 9:

U.S. Patent No. 5,928,150 to Call describes a system for detecting emissions from a radiopharmaceutical injected within a lymph duct wherein a hand-held probe is utilized. When employed to locate sentinel lymph nodes, supplementary features are provided including a function for treating validated photon event pulses to determine count rate level signals. The system includes a function for count-rate based ranging as well as an adjustable ~~thresholding~~ threshold feature. A post-threshold amplification circuit develops full-scale aural and visual outputs.

Paragraph beginning on Page 9, Line 10:

The aim of all such procedures is to pin-point the target area as precisely as possible in order to get the most precise biopsy results, preferably from the most active part of a tumor, or to remove such a tumor in its entirety, ~~on the one hand~~ with minimal damage to the surrounding, non affected tissues~~, on the other hand~~.

Paragraph beginning on Page 9, Line 14:

~~However, in the current state of the prior art this~~ This goal is yet to be achieved, as most of the common imaging modalities such as fluoroscopy, CT, MRI, mammography or ultrasound demonstrate the position and appearance of the entire lesion with anatomical modifications that the lesion causes to its surrounding tissue, without differentiating between the non-active mass from the physiologically active part thereof.

Paragraph beginning on Page 9, Line 20:

~~On the other hand~~ Furthermore, prior art radiation emission detectors and (or) biopsy probes, while being suitable for identifying the location of the radiation site, ~~they~~ leave something to be desired from the standpoint of facilitating the removal or other destruction of the detected cancerous tissue, with ~~minimum invasion of the patient~~ minimal trauma.

Paragraph beginning on Page 9, Line 24:

The combination of modalities, as is offered by the present invention, can reduce the margin of error in ~~positioning~~ locating such tumors. In addition, the possibility of demonstrating the position of the active part of a tumor superimposed on a scan from an imaging modality that shows the organ or tumor, coupled with the possibility to follow a surgical tool in reference to the afflicted area during a surgical procedure will allow for a more precise and controlled surgical procedures to take place, minimizing the aforementioned problems.

Paragraph beginning on Page 9, Line 31:

The present invention addresses these and other issues which are further elaborated hereinbelow, and offers the physicians and patients more reliable targeting, ~~that~~ which in turn will result in less invasive and less destructive surgical procedures and ~~less~~ fewer cases of mistaken ~~diagnosis~~ diagnoses.

Paragraph beginning on Page 10, Line 5:

The present invention successfully addresses the shortcomings of the presently known configurations by providing a radioactive emission probe in communication with a position tracking system and the use thereof in a variety of systems and methods of medical imaging and procedures. Specifically, wide-~~apeture~~ aperture collimation - deconvolution algorithms are provided, for obtaining a high-efficiency, high resolution image of a radioactivity emitting source, by scanning the radioactivity emitting source with a probe of a wide-aperture collimator, and at the same time, monitoring the position of the radioactive emission probe, at very fine time intervals, to obtain the equivalence of fine-aperture collimation. The blurring effect of the wide aperture is then corrected mathematically. Furthermore, an imaging method by depth calculations is provided, –based on the attenuation of photons of different energies, which are emitted from the same source, coupled with position monitoring.

Paragraph beginning on Page 12, Line 14 (underline removed from under "a single dimension):

FIG. 13 is a simplified pictorial illustration of a single dimension image formation with a nuclear radiation probe attached to a position tracking system of the system of Figure 12, in accordance with a preferred embodiment of the present invention;

Paragraph beginning on Page 13, Line 27:

FIGs. 29A – 29B schematically ~~illustrates~~ illustrate the manner of calibrating the handheld probe of FIGs. 28A – 28F, in accordance with a preferred embodiment of the present invention;

Paragraph beginning on Page 14, Line 8:

FIGs. 34A – 34C illustrate endoscopic radioactive emission probes, in accordance with the present invention;

Paragraph beginning on Page 14, Line 9:

FIG. 35 illustrate a method of calculating the depth of a radiation source, in accordance with the present invention; and

Paragraph beginning on Page 14, Line 10:

FIG. 36 illustrate a two-dimensional image of the radioactivity emitting source, produced by a free-hand scanning of a ~~cancerours~~ cancerous prostate gland, ex vivo, in accordance with the present invention.

Paragraph beginning on Page 14, Line 14:

The present invention ~~is of~~ relates to a radioactive emission probe in communication with a position tracking system and the use thereof in a variety of systems and methods of medical imaging and procedures. Specifically, wide- ~~apeture~~ aperture collimation - deconvolution algorithms are provided, for obtaining a high-efficiency, high resolution image of a radioactivity emitting source, by scanning the radioactivity emitting source with a probe of a wide-aperture collimator, and at the same time, monitoring the position of the radioactive emission probe, at very fine time intervals, to obtain the equivalence of fine-aperture collimation. The blurring effect of the wide aperture is then corrected mathematically. Furthermore, an imaging method by depth calculations is provided, based on the ~~attentuation~~ attenuation of photons of different energies, which are emitted from the same source, coupled with position monitoring.

Paragraph beginning on Page 16, Line 15:

It will be appreciated that system 20 of radioactivity emission detector 22 and position tracking system 24 is inherently different from known SPECT and PET imaging systems, as well as from other imaging systems such as X-ray, Mammography, CT, and MRI, since the motion of detector 22 of the present invention is not limited to a predetermined track or tracks, with a respect to an immovable gantry. Rather, detector 22 of the present invention is adapted for a variable-course motion, which may be for example, free-hand scanning, variable-course motion on a linkage system, motion within a body lumen, endoscopic motion through a ~~trucar~~ trocar valve, or another form of variable-course motion.

Paragraph beginning on Page 17, Line 29:

Radioactive emission probes are well known in the art and may use any one of a number of approaches for the determination of the amount of radioactive emission emanating from an object or portion thereof. Depending on the type of radiation, such detectors typically include substances which when interacting with radioactive decay emitted particles emit either electrons or photons in a level which is proportional over a wide linear range of operation to the level of radiation impinging thereon. The emission of electrons or photons is measurable and therefore serves to quantitatively determine radiation levels. Solid-state detectors in the form of N-type, P-type, PIN-type pixellated or unpixellated include, for example, Ge, Si, CdTe, CdZnTe, CdSe, CdZnSe, HgI_2, TlBrI, GaAs, InI, GaSe, Diamond, TlBr, PbI_2, InP, ZnTe, HgBrI, a-Si, a-Se, BP, GaP, CdS, SiC, AlSb, PbO, BiI_3 and ZnSe detectors. Gas (e.g., CO_2 CH_4) filled detectors include ionization chamber detectors, proportional chamber detectors and ~~geiger~~ Geiger chamber detectors. Scintillation detectors include organic ~~scintillators~~ scintillator crystals and liquids, such as $C_{14}H_{10}$, $C_{14}H_{12}$, $C_{10}H_8$, etc., Plastics, NE102A, NE104, NE110, Pilot U and inorganic ~~scintillators~~ scintillator crystals, such as NaI, CsI, BGO, LSO, YSO, BaF, ZnS, ZnO, $CaWO_4$ and $CdWO_4$. Also known are scintillation fiber detectors. Scintillator coupling include photomultiplier tube (PMT) of the following types: side-on type, head-on type, hemispherical type, position sensitive type, icrochannel plate-photomultiplier (MCP-PMTs) and electron multipliers, or photodiodes (and photodiodes arrays), such as Si photodiodes, Si PIN photodiodes, Si APD, GaAs(P) photodiodes, GaP and CCD.

Paragraph beginning on Page 19, Line 3:

Figure 7 shows another example of a radioactive emission probe, a spatially sensitive (~~pixelated~~ pixellated) radioactive emission probe 22" (such as a gamma camera). Detector 22", in effect, includes an array of multitude narrow angle detector units 23. Such an arrangement is used in accordance with the teachings of the present invention to reduce the amount of measurements and angles necessary to acquire sufficient data so as to reconstitute a three-dimensional model of the radioactive object. Examples of spatially sensitive radioactive emission probes employed in a variety of contexts are disclosed in, for example, U.S. Pat. Nos. 4,019,057; 4,550,250;

4,831,262; and 5,521,373; which are incorporated by reference as if set forth herein. An additional example is the COMPTON detector (http://www.ucl.ac.uk/MedPhys/posters/ giulia/giulia.htm). Figure 8 shows a scan optionally made by spatially sensitive radioactive emission probe 22" (such as a gamma camera).

Paragraph beginning on Page 19, Line 15:

A radioactive ~~emmission~~ emission detector of particular advantages for use in context of the present invention is the Compton gamma probe, since, in the Compton gamma probe, spatial resolution is independent of sensitivity and it appears possible to exceed the noise equivalent sensitivity of collimated imaging systems especially for systems with high spatial resolution. The Compton probe is a novel type of gamma-probe that makes use of the kinematics of Compton scattering to construct a source image without the aid of mechanical collimators. Compton imaging telescopes were first built in the 1970s for astronomical observations [V. Schoenfelder et al., Astrophysical Journal 217 (1977) 306]. The first medical imaging laboratory instrument was proposed in the early 1980s [M. Singh, Med. Phys. 10 (1983) 421]. The potential advantages of the Compton gamma probe include higher efficiency, 3-D imaging without detector motion, and more compact and lightweight system. In the Compton gamma probe, high-energy gamma rays are scattered from a first detector layer (or detectors array) into a second detector layer array. For each gamma, the deposited energy is measured in both detectors. Using a line drawn between these two detectors, the Compton scattering equation can be solved to determine the cone of possible direction about this axis on which the gamma ray must have entered the first detector. The intersection of cones from many events is then developed to locate gamma ray sources in the probe's field-of-view. Obviously only coincident events are considered, and the more accurately their energy can be determined, the less uncertainty there is in the spatial angle of the arrival cone. The probe's electronic system is combining coincidence measurements across many detectors and detectors layers with a very good energy resolution. The choice of the geometry and the material of the first layer detector plays a major role in the system imaging capability and depends on (i) material efficiency of single Compton events, in relation to other

interactions; (ii) detector energy resolution; and (iii) detector position resolution. In particular, the overall angular resolution results from the combination of two components, related to the energy resolution and to the pixel volume of the detector.

Paragraph beginning on Page 22, Line 1:

The radioactive emission probe, which can be used in context of the present invention can be a beta emission detector, a gamma emission detector, a positron emission detector or any combination thereof. A detector that is sensitive to both beta and (or) positron and gamma emission can be used to improve localization by sensing for example gamma emission distant from the source and sensing beta or positrons emission closer to the source. A beta detector is dedicated for the detection of either electrons from sources such as ^{131}Iodine, or positrons from sources such as ^{18}Fluorine. A gamma detector can be designed as a single energy detector or as a detector that can distinguish between different types of energies, using the light intensity in the ~~scintilator~~ scintillator as a relative measure of the gamma energy. Also, the detector can be designed to utilize coincidence detection by using detectors facing one another (180 degrees) with the examined organ or tissue in-between. The radiation detector can have different collimators with different diameters. A large bore will be used for high sensitivity with lower resolution while a small bore collimator will have higher resolution at the expense of lower sensitivity.

Paragraph beginning on Page 28, Line 10:

According to a preferred embodiment of the present invention, the surgical instrument is equipped with an additional radioactive emission probe attached thereto or placed therein. This additional detector is used, according to preferred embodiments of the invention, to fine tune the location of radioactive emission from within the body, and in closer proximity to the radioactive source. Since the surgical tool is preferably in communication with a position-tracking system, the position of the additional detector can be monitored and its readouts used to fine tune the position of the radioactive source within the body. Thus, according to this aspect of the present invention, at least one extracorporeal detector and an ~~intracorporealreal~~ intracorporeal detector are used in concert to determine the

position of a radioactive source in the body in highest precision. The extracorporeal detector provides the general position of the source and is used for directing the surgical instrument thereto, whereas the ~~Intracorporeal~~ intracorporeal detector is used for reassuring prior to application of treatment or retrieval of biopsy that indeed the source was correctly targeted at the highest precision.

Paragraph beginning on Page 28, Line 24:

While according to a presently preferred embodiment of the invention two detectors, one extracorporeal and one ~~Intracorporeal~~ intracorporeal, are employed as described above, for some applications a single ~~Intracorporeal~~ intracorporeal detector may be employed, which detector is attached to or integrated with a surgical instrument whose position is tracked.

Paragraph beginning on Page 28, Line 29:

The use of ~~Intracorporeal~~ intracorporeal and extracorporeal detectors calls for careful choice of the radioactive isotope employed with the radiopharmaceutical. While the extracorporeal detector can be constructed with a suitable collimator for handling strong radiation, such as gamma radiation, the ~~Intracorporeal~~ intracorporeal detector is miniature by nature and is limited in design and construction by the construction of the surgical instrument with which it is employed. Since collimators for high energy (80 – 511 KeV) gamma radiation are robust in nature, they are not readily engageable with miniature detectors. Electron (beta) and positron radiation are characterized by: (i) they highly absorbed by biological tissue as they are of lower energy and higher chemical reactivity; and (ii) they are readily collimated and focused by thin metal collimators. It is also possible to use low energy gamma radiation (10 – 30 KeV) for ~~Intracorporeal~~ intracorporeal applications since the collimation of these gamma photons can be achieved with thin layers of Tantalum or Tungsten. As such, the radio pharmaceutical of choice is selected to emit both gamma and beta and (or) positron radiation, whereas the extracorporeal detector is set to detect the high energy gamma radiation, whereas the ~~Intracorporeal~~ intracorporeal detector is set to detect the low energy gamma, beta and (or) positron radiation. Isotopes that emit both high energy gamma and (or) low energy gamma, beta and (or) positron radiation and which

can be used per se or as a part of a compound as radiopharmaceuticals include, without limitation, ^{18}F, ^{111}In and ^{123}I in radiopharmaceuticals, such as, but not limited to, 2-[^{18}F]fluoro-2-deoxy-D-glucose (^{18}FDG), ^{111}In-Pentetreotide ([^{111}In-DTPA-D-Phe^{1}]-octreotide), L-3-[^{123}I]-Iodo-alpha-methyl-tyrosine (IMT), O-(2-[^{18}F]fluoroethyl)-L-tyrosine (L-[^{18}F]FET), ^{111}In-Capromab Pendetide (CYT-356, Prostascint) and ^{111}In-Satumomab Pendetide (Oncoscint).

Paragraph beginning on Page 34, Line 1:

Examples of suitable radiation detectors include a solid state detector (SSD) (CdZnTe, CdTe, HgI, Si, Ge, and the like), a scintillation detector (NaI(Tl), LSO, GSO, CsI, CaF, and the like), a gas detector, or a scintillating fiber detector (S101, S104, and the like)~~, for example~~.

Paragraph beginning on Page 36, Line 31:

In essence, the wide-~~apeture~~ aperture collimation - deconvolution algorithms enable one to obtain a high-efficiency, high resolution image of a radioactivity emitting source, by scanning the radioactivity emitting source with a probe of a wide-aperture collimator, and at the same time, monitoring the position of the radioactive emission probe, at very fine time intervals, to obtain the equivalence of fine-aperture collimation. The blurring effect of the wide aperture is then corrected mathematically.

Paragraph beginning on Page 37, Line 5:

The wide-~~apeture~~ aperture collimation - deconvolution algorithms are described hereinbelow, in conjunction with Figures 27A – 27I, and Figure 22. Experimental results, showing images produced by the wide-~~apeture~~ aperture collimation - deconvolution algorithms of the present invention, in comparison to a conventional gamma camera are seen in Figures 23A – 26B, and Figure 36, hereinbelow.

Paragraph beginning on Page 42, Line 3:

One problem of using estimates (5) (besides computational problems if the dimension m of the space H is very large) is that the operator $M: H \rightarrow H$ of the form

(3) is "bad ~~invertable~~ invertible". In other words, the estimation problem is "ill-posed". It means that having a noise ε_k in the measurements scheme (3), even if the noise is small, may sometimes result in a very large estimation error dist(I , Î).

Paragraph beginning on Page 42, Line 8:

This means that the estimation problem requires additional regularization. This is a general problem of solving a large set of linear equations. There are several methods for solving such equations. Below is described one of the known methods for solving such equations but numerous other methods are also possible, theses include gradient decent methods such as in (http://www-visl.technion.ac.il/1999/99-03/www/) and other methods that are generally known in the art. Further, it is possible to improve the image reconstruction by taking into account the correlation between measurements as they are done with substantial overlap. Also, in the following description, a regular step function is assumed for the representation of the pixels or voxels, other basis may be used such as wavelet basis, ~~gaussian~~ Gaussian basis, etc., which may be better suited for some applications.

Paragraph beginning on Page 42, Line 21:

Let $\varphi_1, \varphi_2, \ldots, \varphi_m$ be eigenvectors of operator $M: H \to H$ corresponding to ~~eigenvalues~~ Eigenvalues $\lambda_1 \geq \lambda_2 \geq \ldots \geq \lambda_m \geq 0$.

Paragraph beginning on Page 46, Line 16:

The algorithms described herein are applicable not only to the analysis of readings obtained using a directional radioactivity detector, rather they also apply for spatially sensitive (~~pixelated~~ pixellated) radioactivity detectors. In this case, the readings of each pixel are algorithmically treated as described herein like for a directional radioactivity detector. The motivation behind using a spatially sensitive detector is to save on measurement time by receiving readings from a multitude of directions in parallel. This, in essence, creates a number of overlapping low resolution images which can then be processed to form a high resolution image. In addition, the spatially sensitive detector can be scanned to improve even further the resolution using the algorithms described hereinabove.

Paragraph beginning on Page 49, Line 12:

As seen in Figure 28E, each cell 705 may include a plurality of radiation detector pixels 703, formed for example, as square pixels of 5 X 5 mm and length L1 also of ~~bout~~ about 5 mm. The reason for the division of nuclear detector 708 into pixels 703 is that while the wide aperture of a coarse collimator increases the counting efficiency, radiation detector uniformity is better maintained when the size of the radiation detectors is small. Thus, it is desired to combine a coarse collimator grid with a fine pixel size. Lead spacers are placed between the pixels. From spatial resolution consideration, each cell 705 preferably operates as a single pixel, but each pixel 703 within cell 705, must be calibrated individually, to correct for material nonuniformity, as will be described hereinbelow, in conjunction with Figure 29B.

Paragraph beginning on Page 52, Line 5:

Referring further to the drawings, Figures 29A – 29B schematically illustrate the manner of calibrating handheld probe 700, in accordance with preferred embodiments of the present invention. Non-uniformity of the material leads to different ~~sensitivies~~ sensitivities for each pixel. A correction is required to eliminate the sensitivity effect of the different pixels.

Paragraph beginning on Page 53, Line 1:

During ~~aquistion~~ acquisition, the sum of counts within the bounded windows of all pixels in cell 705(n) is multiplied by the ~~the~~ correction factor for that cell 705(n) to obtain a sensitivity corrected count rate.

Paragraph beginning on Page 55, Line 13:

Referring further to the drawings, Figures 34A – 34C schematically illustrate endoscopic radioactive emission probes 800, adapted to be inserted into the body, on a shaft or a catheter 713, via a ~~trucar~~ trocar valve 802 in a tissue 810.

Paragraph beginning on Page 55, Line 31:

Referring further to the drawings, Figure 35 schematically illustrates a manner of calculating a distance, d, between radioactive emission probe, such as probe 700 (Figures 28A – 28F) and a radiation source 766, based on the attenuation of photons of different energies, which are emitted from the same source. Probe 700 is on an extracorporeal side 762 and radiation source 766 is on an ~~Intracorporeal~~ intracorporeal side 764 of a tissue 768.

Paragraph beginning on Page 58, Line 3:

It will be appreciated that by calculating the depth of a radiation source at each position, one may obtain a radiation source depth map, in effect, a three-dimensional ~~iamge~~ image of the radiation source. This information may be superimposed on the radiation source image, as produced by other methods of the present invention, as an independent check of the other methods. For example, a radiation source image produced by the wide-aperture collimation – deconvolution algorithms may be superimposed on a radiation source image produced by depth calculations of based on the attenuation of photons of different energies.

Paragraph beginning on Page 60, Line 21:

The radioactivity detector can be mounted on a catheter that is entered through the blood vessels to the heart to evaluate ischemia from within the heart in order to guide ablation probes or another type of treatment to the appropriate location within the heart. Another application which may benefit from the present invention is the localization of blood clots. For example, a radioactivity detector as described herein can be used to asses and differentiate between new clots and old clots. Thus, for example, the radioactivity detector can be placed on a very small caliber wire such as a guide wire that is used during PTCA in order to image blood-vessel clots. ~~Intrabloodvessel~~ Blood-vessel clots can be searched for in the aortic arc as clots therein are responsible for about 75 % of stroke cases.